

1 Background

One of the unique properties of **diffusion imaging tractography** is its ability to perform **individualized** tract delineations for each subject.

- Avoids mis-registration issues.
- Especially valuable for clinical/patient studies because analogous tracts can be examined even in the presence of gross brain abnormalities.

However, despite the eloquence of this technique, the intricate personalized **tract dissections are typically collapsed down** for statistical analyses.

- Ignores the potentially rich anatomical variation in diffusion imaging metrics along the tracts (**Fig. 1**).
- Yields **only a single mean DTI metric estimate** for each tract and for each subject (see red point-spread estimate in **Fig. 6**).
- Results in suboptimal detail for brain mapping studies, and also implies reduced power to detect group differences within patient populations.
- Subtle **differences may be averaged** out across the whole tract, and the **variance estimates could be inflated** because the potential along-tract variance is ignored.

To address this limitation, there is interest in developing methods with **greater within-tract detail**.¹⁻³

We have developed a **toolkit for along-tract analysis**.

- Allows analysis at many cross sections along white matter tracts.
- **Increased detail** for brain mapping studies and **increased power** for clinical studies.
- Written in MATLAB and R; uses the TrackVis framework.

2 Processing flow

1. Perform tract dissections

- Ex: Manual "cookbook" ROIs (**Fig. 2**).^{4,6}

2. Determine along-tract properties

- Instead of collapsing the entire tract into 1 value, model the scalar properties (FA, etc.) at many cross-sections *along* the tract (**Fig. 3**).
- Streamlines modeled using **cubic B-splines** (**Fig. 4**).
- Streamlines resampled to give uniform number of vertices for each streamline.
- The mean FA and variance is estimated at each cross-section along the tract.

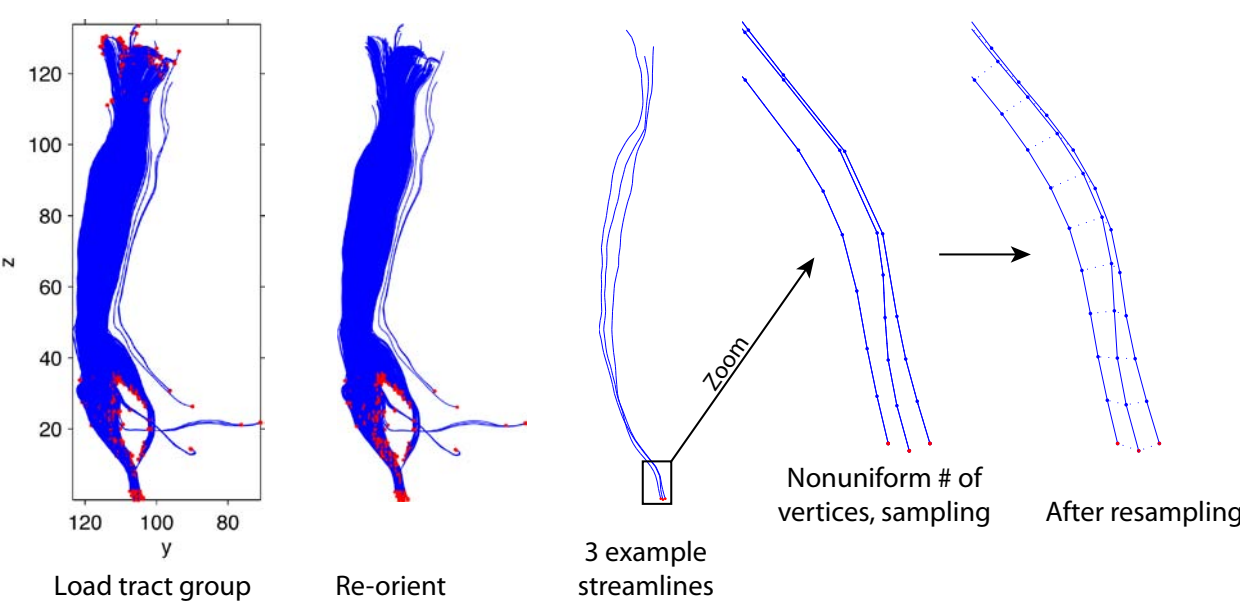


Fig. 3: Basic along-tract processing workflow.

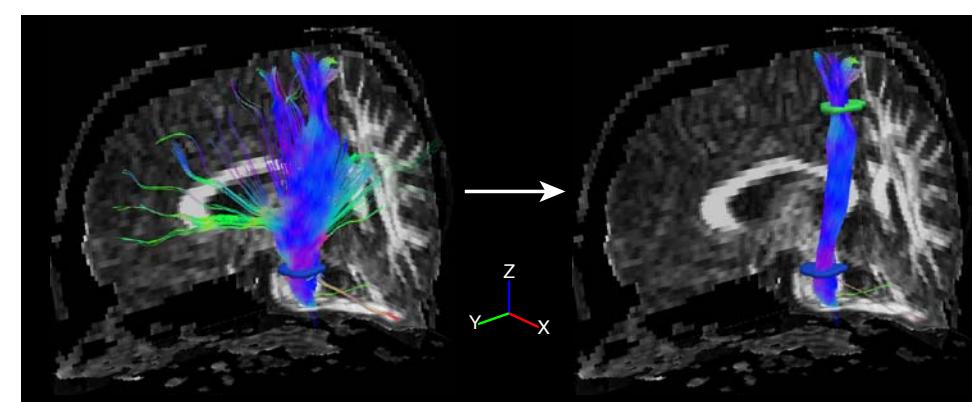


Fig. 2: Tract group dissections.

```
for each Subject
  for each Tract
    for each Hemisphere
      Load tract group
      Reorient streamlines
      Interpolate streamlines
      Extract scalars
      Collapse scalars cross-sectionally
    end
  end
end
```

(*trk_read*)
(*trk_flip*)
(*trk_interp*)
(*trk_add_sc*)
(*trk_mean_sc*)

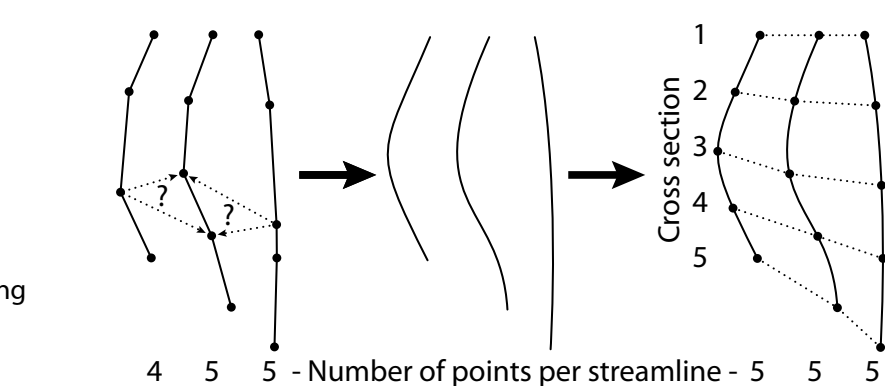


Fig. 4: B-spline resampling

3. Statistical analysis

Simple **mixed effects model** can be used for each tract to determine if there is an overall shift in the FA vs. position curve, and/or localized regions of group differences within the tract (ANOVA).

- **FA ~ 1 + Position + Point + Group:Position**

- Subject-level random effect included to account for the repeated measures.

- **Permutation methods** used to control type 1 error rate across all tracts/hemispheres (**Fig. 5**).

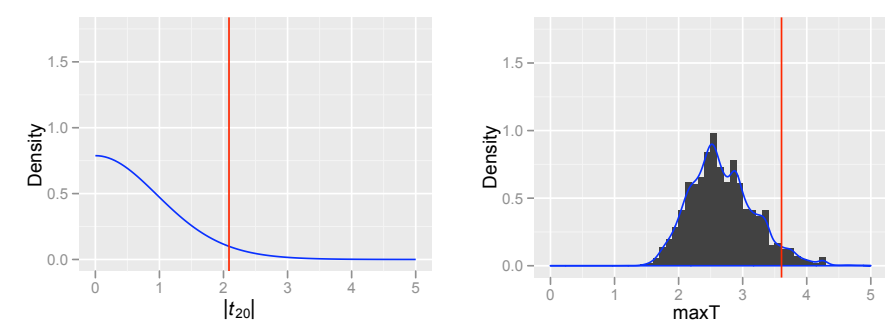


Fig. 5: (Left) Theoretical *t* distribution and *p* < 0.05 critical value. (Right) Empirical distribution of the maximum *t* statistic across all comparisons.

4. Summarize results

- 2D statistical graphics
- 3D overlays to visualize effect sizes and *p*-values

3 Within-subject analysis

- Left corticospinal tract (CST) analyzed along its length.
- Tract-averaged FA estimate: 0.58 ± 0.13
- **Along-tract** modeling reveals:
 - FA variations within the tract (**Fig. 6**).
 - Less unexplained variance (Compare to red tract-averaged estimate in **Fig. 7**).

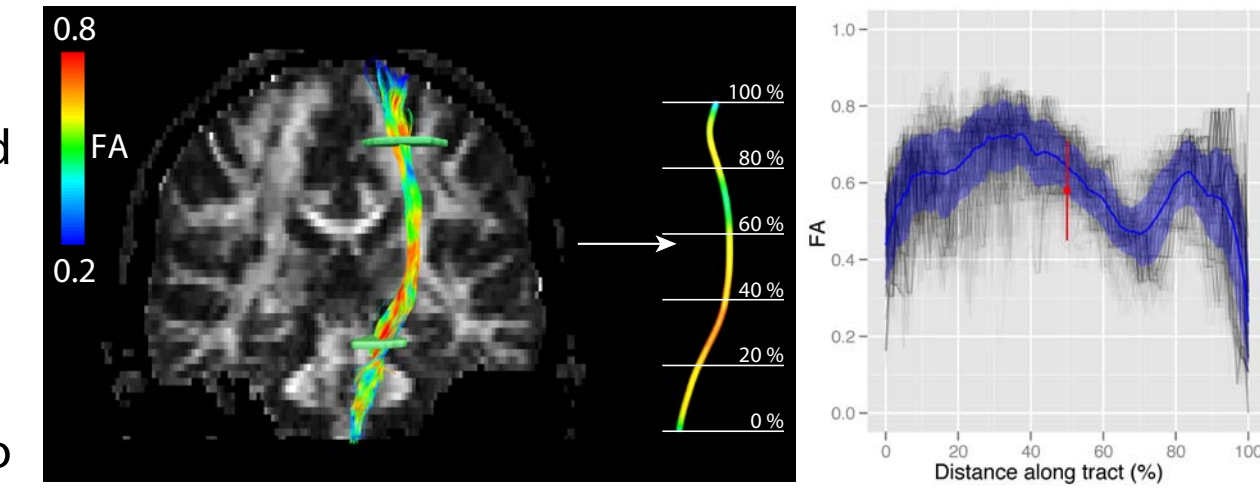


Fig. 6: Example along-tract analysis in the left corticospinal tract.

4 Between-group analysis

• Fetal Alcohol Spectrum Disorders (FASDs):

- Neurological/cognitive problems cause greatest long-lasting morbidity.
- Previous findings of ↓ regional volumes, but ↑ cortical thickness, suggest white matter abnormalities may be an important contributor.⁵
- Previous **voxel-wise** and **tract-averaged** studies have shown ↓ white matter integrity in corpus callosum, and fronto-temporal regions.⁵
- Along-tract methods may:
 - Contribute added detail to localize previously observed differences.
 - Reveal previously-unknown focal effects.
 - Allow for easier comparison between studies.

Results summarized in **data-rich statistical graphics** (**Fig. 8**):

- 6 dimensions
- Allows you to explore many different questions:
 - How do the DTI properties vary along the tracts?
 - Do these patterns differ with respect to: Group? Tract? Hemisphere?
 - Do the DTI properties relate to the number of streamlines?
 - Outliers?
- Allows you to shift your focus to different levels within the data:
 - Raw sample distributions
 - Statistical summaries
 - Results of hypothesis testing (Group offset? Localized within-tract effects?)

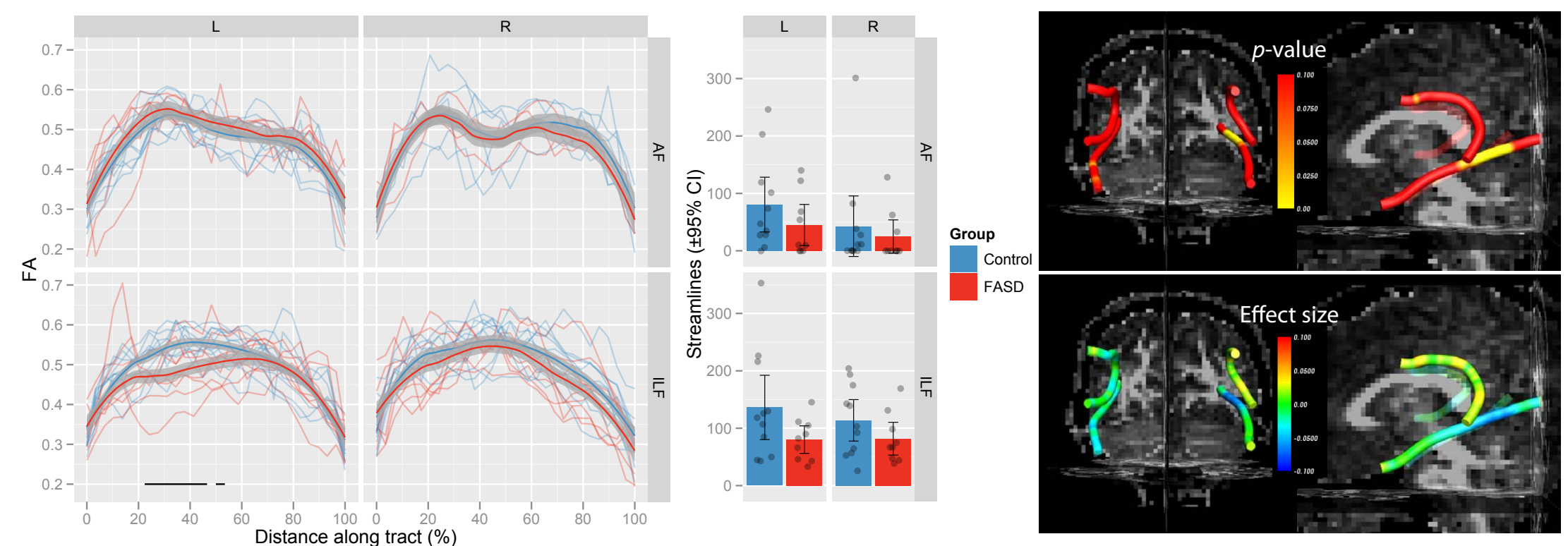


Fig. 8: Example between-group along-tract analysis, comparing FASD subjects and controls.

Fig. 9: Example between-group along-tract analysis, comparing FASD subjects and controls.

Results can also be **visualized** on an example subject's mean tract geometry (**Fig. 9**).

- Allows for more direct comparison with voxelwise results.

5 Conclusion

Along-tract analysis techniques reveal a much **richer data landscape** than what is typically utilized by traditional tractography methods.

- This **can enhance a wide range of connectivity analyses** utilizing a variety of underlying diffusion models.

6 References

1. Corouge I, Fletcher P.T., et al., 2006. Fiber tract-oriented statistics for quantitative diffusion tensor MRI analysis. *Med. Image Anal.* 10, 786–98.
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